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IN THE UNITED STATED PATENT AND TRADEMARK OFFICE

Appl. No.	:	09/807,402
Applicant	:	Hofert et al.
Filed	:	August 3, 2001
Title	:	COMBINATION OF GESTAGENS AND SUGARS
TC/A.U.	:	1623
Examiner	:	L. C. Maier
Docket No.	:	SCH-1808

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

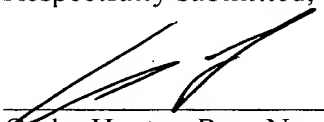
SUPPLEMENTAL REPLY

Sir:

Further to the Reply filed on September 27, 2004, attached is the declaration discussed therein.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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Date: November 4, 2004

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DECLARATION UNDER 37 C.F.R. §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Thomas Backensfeld, being duly warned, declare that:

I am a listed inventor of the above-captioned application and am, therefore, familiar with the invention described therein and with the grounds for rejection made against the claims of the application in the Office Action mailed January 26, 2004, from the U.S. Patent and Trademark Office.

My expertise for making this declaration is demonstrated in the attached CV. If a patent issues from this application and if it is decided by the assignee to pursue a commercial product falling under its claims and if such a commercial product is approved by FDA and sold in the US, then under German law, I and the other inventors will receive some income derived from such sales.

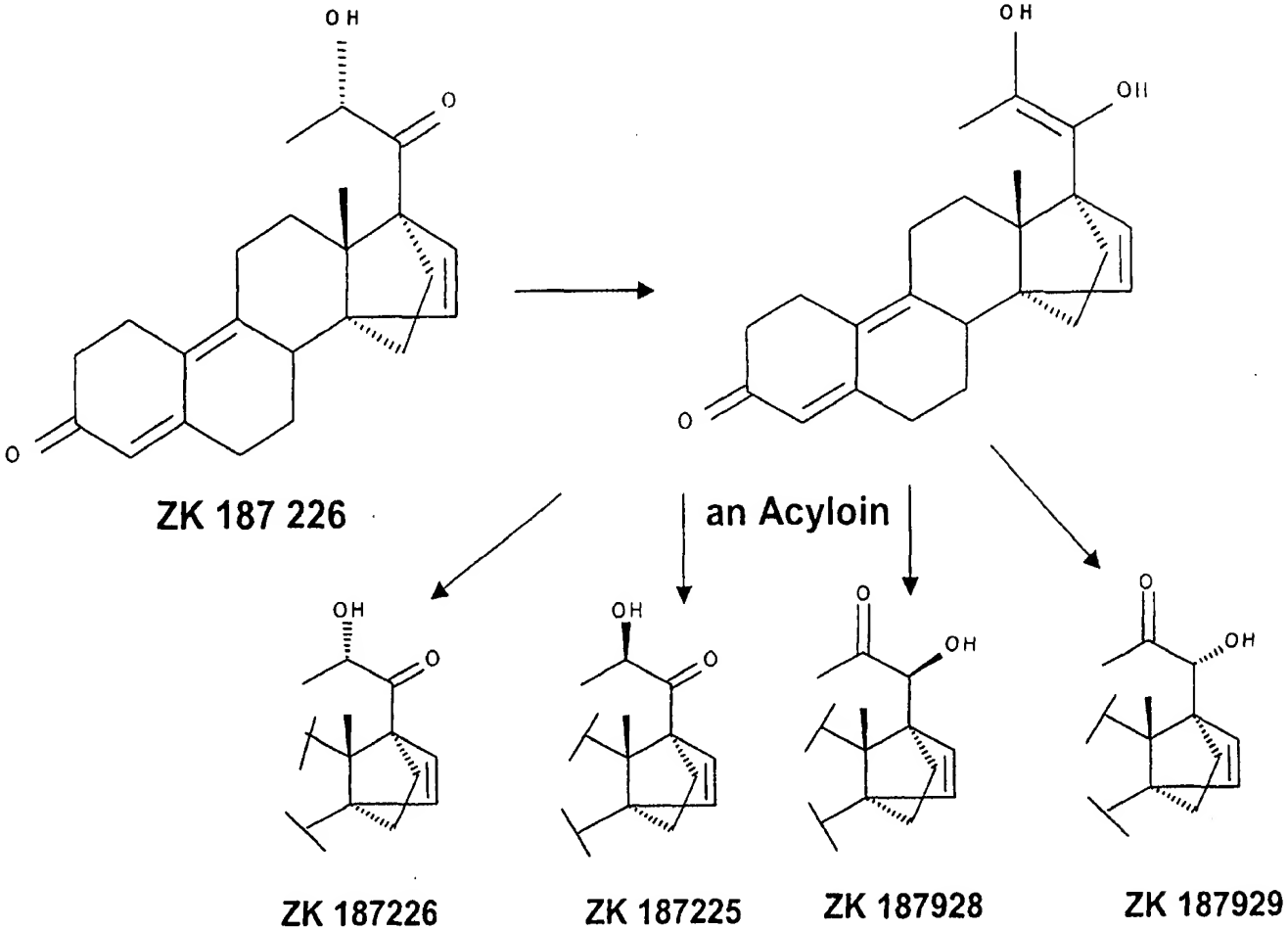
The following experiments were conducted by me or under my supervision.

Compounds of formula I of the claims are subject to acyloin rearrangement during storage, in which case variants occur as discussed in the specification of this application. ZK 187226 is a compound of the invention and has the chemical structure illustrated on page 2. (This compound is a tautomer existing in the (H, OH) or (=O) forms, as shown.) Page 2 also illustrates acyloin rearranged variants of the compound ZK 187226, identified as ZK 187225, ZK 187928 and ZK 187929.

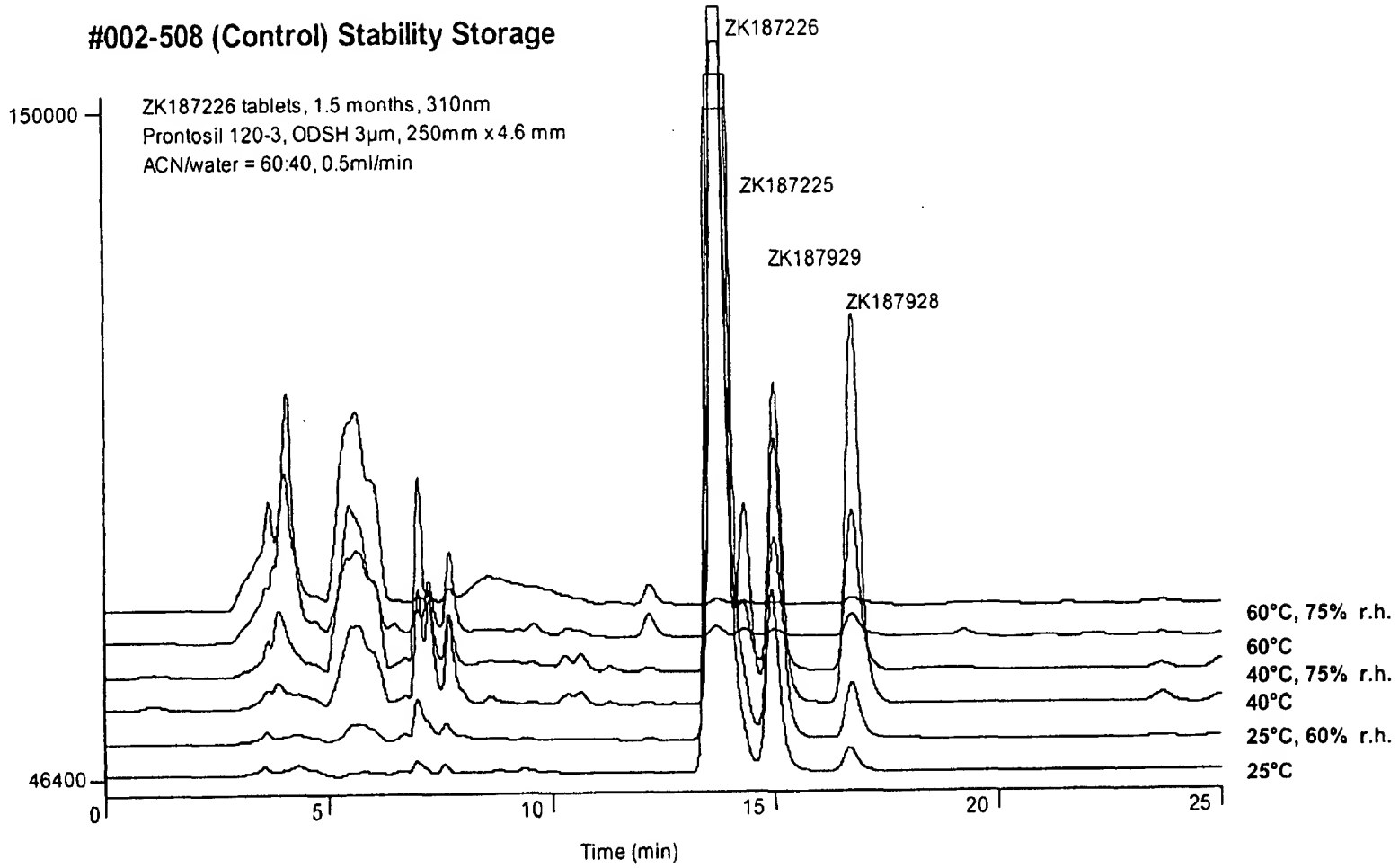
Side-by-side storage stability comparative tests of tablets containing ZK 187226 are conducted without and with the presence of β-cyclodextrin in the tablets. The results are depicted in HPLC chromatograms on pages 3 and 4, respectively, and are identified as (Control) and (β-CD-Clathrate), respectively. The tablets were stored for 1,5 months under a variety of conditions identified on the chromatograms, i.e., -18°C; 25°C; 25°C, 60% r.h.; etc. (where "r.h." means relative humidity).

Decomposition Pathway

Decomposition Pathway: Acyloin Rearrangement

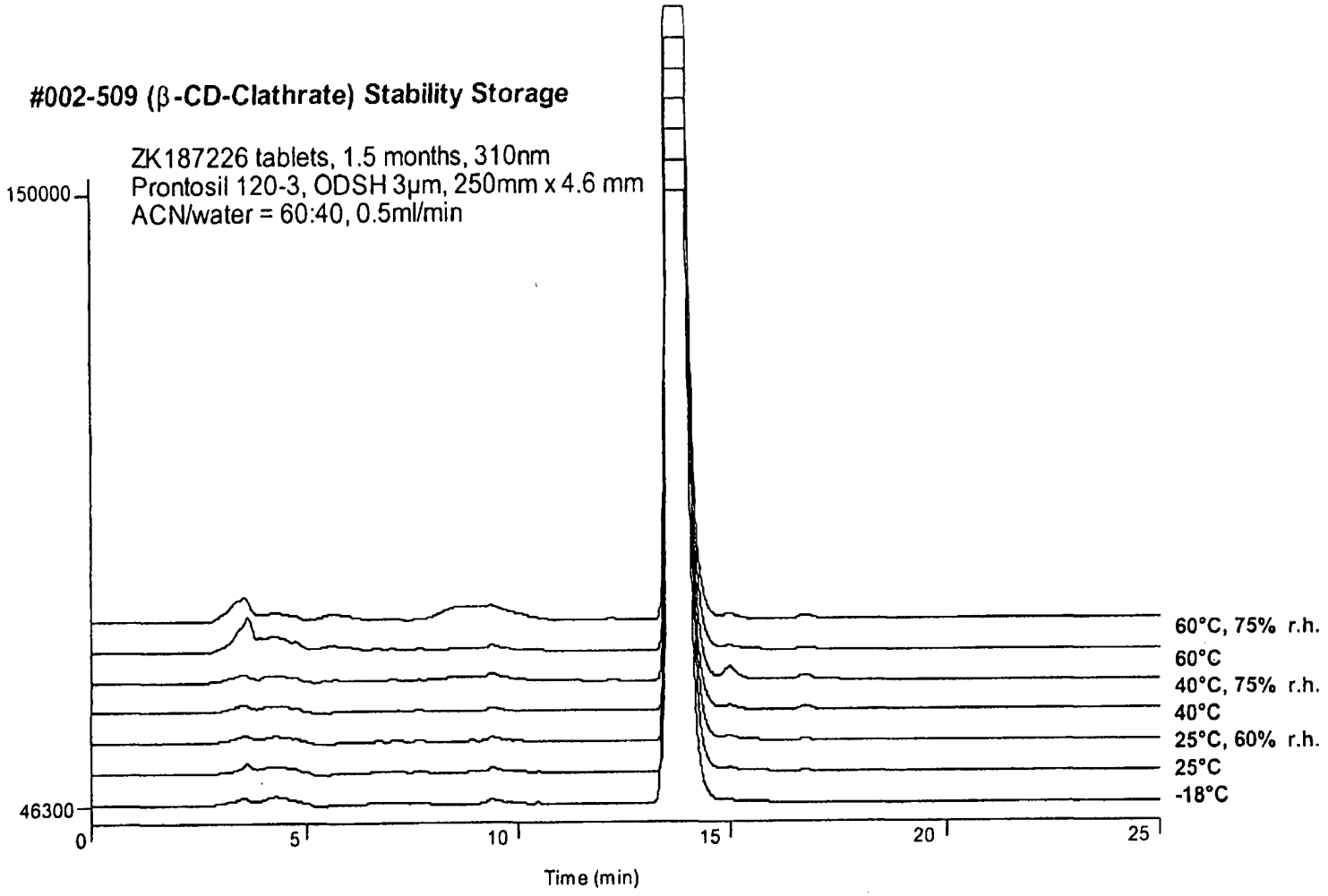


HPLC Chromatogram



ZK 187226

HPLC Chromatogram



ZK 187226

The chromatogram on page 3, where no β-cyclodextrin is present in the tablets, shows a number of peaks for compounds other than ZK 187226, including significant peaks for each of the acyloin rearranged variants of the compound ZK 187226, especially at higher temperatures and relative humidity.

The chromatogram on page 4, where β-cyclodextrin is present in the tablets, shows no significant peaks for compounds other than ZK 187226, meaning that acyloin rearrangement of ZK 187226 was prevented by the addition of β-cyclodextrin to the tablets.

The test results demonstrate that compounds of formula I in tablets according to the claims are significantly more stable than tablets that do not contain β-cyclodextrin and that β-cyclodextrin stabilized ZK 187226 from degradation through acyloin rearrangement, which was not expected from the prior art. Acyloin rearrangement represents a significant degradation mechanism as significant size peaks are present for the acyloin rearranged variants of ZK 187226. Accordingly, the results are significant and would not have been expected by those in this field from the disclosure of Backensfeld or otherwise.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Thomas Backensfeld 10/25/2004

Thomas Backensfeld Date

Curriculum Vitae
Dr. Thomas Backensfeld

Personal

Name:	Dr. Thomas Backensfeld
Place of residence:	D - 13127 Berlin
Date of birth:	22.12.1959
Marital Status:	married, 2 children
Nationality:	German
High School:	1979
Military Service:	1979 - 1980
Occupation:	Pharmacist
Language:	German, English (French and Japanese basics)

Professional

1980 - 1984:	University of Münster, Germany - Study of Pharmaceutical Sciences
1985:	Practical education in pharmacy (public pharmacy; hospital pharmacy)
1886 - 1990:	University of Kiel, Germany - PhD thesis in Pharmaceutics and training of students
1990, Nov. 01:	Schering AG, Berlin
1990 - 1992:	Head of analytical working group in 'Pharma Labor' department: Analytics of all kind of dosage forms
1992 - 2001:	Head of formulation working group in 'Oral Dosage Formulation' department: Preformulation, Formulation and Manufacturing of all kind of oral dosage forms
1996:	Pharmacuetical Development - group leader in formulation development group
2001:	Head of formulation development group in 'Oral Dosage Formulation' department
2002:	Head of 'Production of Highly Potent Drugs / Bulk Weighing' department: Plant manager